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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
BJ Forman	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 1-15 considered unpatentable for the reasons indicated below:

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 7, lines 32-34). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

First paragraph of 35 U.S.C. 112: Written Description

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to an array of probes comprising probes complementary to a known reference sequence wherein the reference sequence includes at least 90% of the human genome.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention.

Reduction to practice

The specification does not describe an actual reduction to practice of the claimed invention. The specification teaches that the number of probes ranges from 5 to 1,000,000 (page 35, lines 37-38) wherein the targets are from "regions of the genome" e.g. expressed or non-expressed sequences (page 8, lines 2-9). The specification further teaches that 300 array having 1Mb/array are required to analyze "**10%** of a mammalian genome" (page 14, lines 7-9). As such, a single array cannot comprise probes complementary to a known reference sequence wherein the reference sequence includes at least 90% of the human genome. Therefore, Applicant has not reduced the claimed array to practice.

Completed by drawings

The specification does contain drawings. As such, the drawings cannot illustrate that Applicant was in possession of the claimed array.

Description of identifying characteristics

The specification has not been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention. While the specification teaches that 300 arrays having 1Mb/array are required to analyze "**10%** of a mammalian genome" (page 14, lines 7-9) the specification has not attempted to teach or describe identifying characteristics of an array comprising probes complementary to at least 90% of the human genome as claimed, the specification has not

For the reasons stated above, the specification does not provide a written description of the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.
The courts have stated that the specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonable conclude the inventor had possession of the claimed invention see *In re Vas-Cath*, Inc. 935F2d. 1555, 1563, 19 USPQ2d 1111,1116

Second paragraph of 35 U.S.C. 112: Indefinite

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-14 are indefinite in Claim 1, step (b) for the recitations "the sequence and "the probe array" because the recitations lack proper antecedent basis in the claim. It is noted that step (a) and line 1 of step (b) recites "array of probes". However, "probe array" and "array of probes" differ in scope.

Claims 1-14 are further indefinite in Claim 1, step (c) for the recitation "the relative hybridization" because the recitations lack proper antecedent basis in the claim. It is suggested that Claim 1 be amended to provide proper antecedent basis.

Claim 15 is indefinite for the recitation "the hybridization pattern" because the recitation lacks proper antecedent basis in the claim. It is suggested that the claim be amended to provide proper antecedent basis.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Preliminary Comments

The claims are drawn to a method for analyzing a target nucleic acid comprising the

reference sequence and (e) providing a further array of probes comprising probes complementary to the estimated sequence of the target nucleic acid. In view of the open claim language "comprising", the array of probes for step (e) encompasses any and all probes in the array of probes for step (a). As such, hybridization to the same "array" is encompassed buy the open claim language. Furthermore, the claims are drawn to an array of probes but does not require the probe be immobilized and arrayed onto a solid support.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

8. Claims 1, 3, 5-8 and 12-15 are rejected under 35 U.S.C. 102(a) as being anticipated by Kozal et al (Nature Medicine, 07 July 1996 2: 753-759).

Regarding Claim 1, Kozal et al disclose a method of analyzing a target comprising designing an array of probes, not comprising every possible probe of a given length, but comprising a probe set complementary to a known reference sequence (e.g. PR gene), hybridizing the target to the array wherein the target is a variant of the reference (i.e. "extremely variable" USA HIV-1 clade B proteases, Abstract) determining relative hybridization of the probes to the target and estimating the sequence of the target (page 757, lines 1-8 and Fig 5b, left most quadrant containing 11, 14, 17 and 20 base probes) and providing a further array of probes comprising a probe set comprising probes complementary to the estimated sequence (Fig 5b, second quadrant from the left containing 11, 14, 17 and 20 base probes overlapping with the probes is the left quadrant).

Figure 5 illustrates the PR chip and figure 5(b) specifically illustrates 5 different hybridization reactions wherein at each hybridization loci, the sequence of the target is estimated and at each subsequent hybridization loci, the sequence is re-estimated. The hybridization and sequence re-estimation is repeated until each base is determined thereby analyzing the target (page 756-757). It is noted that the claims do not require separate, distinct and/or sequential probe preparation or hybridization steps. Step (e) merely requires that the array comprises probes complementary to the estimated sequence. This recitation encompasses the same array with the same probes as step (b) because the array of step (b) comprises probes complementary to the estimated sequence.

Regarding Claim 3, Kozal et al disclose the method wherein the target is a species variant of the reference (i.e. variant of the USA HIV-1 clade B proteases, Abstract)

Regarding Claims 5-6, Kozal et al disclose the method wherein the target shows 80-95% identity with the reference (i.e. the analyzed targets differ from the reference 382 base region by 9, 6, 3 and 4 bases, page 754, Table 1 spanning page 755, first paragraph).

Regarding Claim 7, Kozal et al disclose the method wherein the reference sequence is at least 1000 nucleotides long i.e. 1040 bases of the HIV-1 pol gene (page 758, left column, second full paragraph) wherein the probe set and array comprises overlapping probes perfectly complementary to and spanning the reference (Fig 5, the first and second quadrant contain 11, 14, 17 and 20 base overlapping probes, page 757, lines 1-8).

Regarding Claim 8, Kozal et al disclose the method wherein an estimated sequence includes a nucleotide whose identity is ambiguous and the probe set includes a probe having nucleotides aligned with the position of ambiguity i.e. each base is deemed ambiguous in the method of Kozal and a probe set is designed for each base whereby each probe set comprises a probe having a different nucleotide at the specific base position (Fig. 5, page 757).

Regarding Claim 12, Kozal et al disclose the method wherein the array comprises a first probe set comprising a plurality of probes, each comprising a segment of at least 6 nucleotides

complementary to a subsequence of the reference and at least one interrogation position (Fig. 5B, first quadrant on the left, and page 757, lines 1-8) and second, third and fourth probe sets each comprising a corresponding probe for each probe in the first set and identical to at least 6 nucleotides of the sequence from the first probe set except that at least one interrogation position is occupied by a different nucleotide (see overlapping probe design, Fig. 3).

Regarding Claim 13, Kozal et al disclose the method wherein the sequence is estimated by comparing relative binding of four corresponding probes from the four probe sets, assigning a nucleotide as the complement of the interrogation position having the greatest specific binding and repeating until each nucleotide has been estimated (page 756-757).

Regarding Claim 14, Kozal et al disclose the method wherein the target differs from the reference by at least two positions within a probe (page 757, last two paragraphs).

Regarding Claim 15, Kozal et al disclose a method of analyzing a target nucleic acid comprising designing an array of probe complementary to an estimated sequence of a target wherein the array does not contain every possible probe of a given length, hybridizing the array to the target to determine a re-estimated sequence of the target from the hybridization pattern and repeating the hybridization and determining for each region on the array wherein each region on the array represents each base of the reference sequence (pages 756-757). Kozal et al teach the method wherein the array of probes is designed by providing probes complementary to a reference sequence. The reference sequence is the estimated sequence because Kozal estimates the target is complementary, at least in part, to the reference sequence. Kozal hybridizes to probe set at a first quadrant of the array and re-hybridizes the target subsequent quadrants on the array. From the first hybridization at the first quadrant, differences between the reference and target sequences are determined whereby the target is (re)estimated. The hybridization and re-estimation are repeated thereby providing the target sequence.

9. Claim 15 is rejected under 35 U.S.C. 102(e) as being anticipated by Skeina (U.S. Patent No. 5,683,881, filed 20 October 1997).

Regarding Claim 15, Skiena discloses a method of analyzing a target nucleic acid comprising designing an array of probe complementary to an estimated sequence of the target wherein the array does not contain every possible probe of a given length (Claim 1, step d), hybridizing the array of probes to the target, determining a re-estimated sequence of the target from the hybridization and repeating the designing, hybridizing and determining (Column 4, lines 5-67 and Claim 2).

10. Claims 1-3, 5-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Chee et al (WO 95/11995, published 4 May 1995).

Regarding Claim 1, Chee et al disclose a method of analyzing a target comprising designing an array of probes, not comprising every possible probe of a given length, but comprising a probe set complementary to a known reference sequence (page 18, lines 2-12 and 25-28), hybridizing the target to the array wherein the target is a variant of the reference determining relative hybridization of the probes to the target (e.g. page 12, lines 24-page 13, line 8; Fig 12; and page 30, lines 3-20) and estimating the sequence of the target (i.e. sampling each nucleotide of interest several times to call a nucleotide at position, page 18, lines 19-23) and providing a further array of probes comprising a second probe set comprising probes

complementary to the estimated sequence (e.g. to sample adjacent nucleotides of the reference sequence, page 18, lines 21-23 i.e. tiled probe sets (page 21-33) and re-estimating the sequence from the relative hybridization i.e. the sequence is estimated at each position whereby all estimation at all positions subsequent to the first estimation are "re-estimations" of the sequence, e.g. page 8, line 16-page 9, line 11 and page 71, line 30-page 72, line 24).

Regarding Claim 2, Chee et al disclose the method wherein the steps are repeated until the re-estimated sequence is constant between cycles (i.e. sample several times to achieve a high degree of confidence (page 18, lines 19-21)

Regarding Claim 3, Chee et al disclose the method wherein the target is a species variant of the reference (page 18, lines 2-4)

Regarding Claims 5-6, Chee et al disclose the method wherein the target shows 80-95% identity with the reference (page 19, lines 11-14).

Regarding Claim 7, Chee et al disclose the method wherein the reference sequence is at least 1000 nucleotides long (page 20, line 36-page 21, line 8) wherein the probe set and array comprises overlapping probes perfectly complementary to and spanning the reference (i.e. tiled probes: page 3, lines 6-30; page 11, lines 21-26; and Fig. 3).

Regarding Claim 8, Chee et al disclose the method wherein an estimated sequence includes a nucleotide whose identity is ambiguous and the probe set includes a probe having nucleotides aligned with the position of ambiguity i.e. each base is deemed ambiguous in the method of Kozal and a probe set is designed for each base whereby each probe set comprises a probe having a different nucleotide at the specific base position (page 30, lines 3-33).

Regarding Claim 9-11, Chee et al disclose the method wherein the reference sequence is at least 10kb, 1000kb or at least 90% of the human genome (page 20, line 36-page 21, line 8).

Regarding Claim 12, Chee et al disclose the method wherein the array comprises a first

complementary to a subsequence of the reference and at least one interrogation position and second, third and fourth probe sets each comprising a corresponding probe for each probe in the first set and identical to at least 6 nucleotides of the sequence from the first probe set except that at least one interrogation position is occupied by a different nucleotide (page 26, line 2-page 27, line 19).

Regarding Claim 13, Chee et al disclose the method wherein the sequence is estimated by comparing relative binding of four corresponding probes from the four probe sets, assigning a nucleotide as the complement of the interrogation position having the greatest specific binding and repeating until each nucleotide has been estimated (page 30, line 3-33).

Regarding Claim 14, Chee et al disclose the method wherein the target differs from the reference by at least two positions within a probe (page 37, lines 10-38 and Fig. 7).

Regarding Claim 15, Chee et al disclose a method of analyzing a target comprising designing an array of probes, not comprising every possible probe of a given length, but comprising a probe set complementary to an estimated sequence e.g. reference sequence (page 18, lines 2-12 and 25-28), hybridizing the target to the array wherein the target is a variant of the reference determining relative hybridization of the probes to the target (e.g. page 12, lines 24-page 13, line 8; Fig 12; and page 30, lines 3-20) and estimating the sequence of the target (i.e. sampling each nucleotide of interest several times to call a nucleotide at position, page 18, lines 19-23) and repeating the designing, hybridizing and determining i.e. the sequence is estimated at each position whereby all estimation at all positions subsequent to the first estimation are "re-estimations" of the sequence, e.g. page 8, line 16-page 9, line 11 and page 71, line 30-page 72, line 24).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al (WO 95/11995, published 4 May 1995) in view of Dietrich et al (U.S. Patent No. 5,861,243, filed 12 October 1990).

Regarding Claim 4, Chee et al disclose a method of analyzing a target comprising designing an array of probes, not comprising every possible probe of a given length, but comprising a probe set complementary to a known reference sequence (page 18, lines 2-12 and 25-28), hybridizing the target to the array wherein the target is a variant of the reference determining relative hybridization of the probes to the target (e.g. page 12, lines 24-page 13, line 8; Fig 12; and page 30, lines 3-20) and estimating the sequence of the target (i.e. sampling each nucleotide of interest several times to call a nucleotide at position, page 18, lines 19-23) and providing a further array of probes comprising a second probe set comprising probes complementary to the estimated sequence (e.g. to sample adjacent nucleotides of the reference sequence, page 18, lines 21-23 i.e. tiled probe sets (page 21-33) and re-estimating the sequence from the relative hybridization i.e. the sequence is estimated at each position whereby all estimation at all positions subsequent to the first estimation are "re-estimations" of the sequence, e.g. page 8, line 16-page 9, line 11 and page 71, line 30-page 72, line 24). Chee et al further teach the reference sequence is one of interest having clinical significance in human patients e.g. HIV (page 19, lines 16-19). However, Chee et al do not specifically teach a

However, comparison of human reference sequence and primate target sequence was well known in the art at the time the claimed invention was made as taught by Dietrich et al who teach that primates are a desired animal model for the study of HIV genotherapeutics (Column 3, lines 39-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the human reference sequence and primate target sequence taught by Dietrich et al to the study of genomic sequences having clinical significances taught by Chee et al (page 19, lines 16-19) based on the teaching of Dietrich et al wherein the primate is the desired animal model for the study of HIV genotherapeutics (Column 3, lines 39-50).

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Primary Examiner
Art Unit: 1634
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